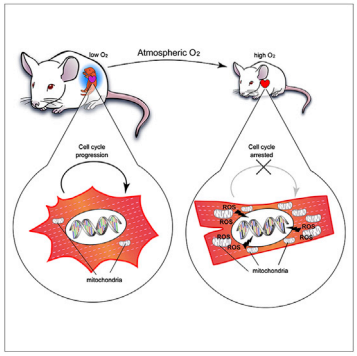
In This Issue

Cell



Oxygen Dilemma

PAGE 565

One of the mysteries of cardiac biology is the incessant cell-cycle arrest of adult mammalian cardiomyocytes. Puente et al. show that the increase in environmental oxygen after birth induces cardiomyocyte cell-cycle arrest through oxidative DNA damage. The embryonic mammalian heart and the regenerative zebrafish hearts are exposed to a relatively hypoxic environment, while the postnatal mammalian heart trades its regenerative capacity for oxidative energy efficiency.

Blood, Sweat, and Tears Beget Blood

PAGE 549

Hematopoietic stem cells (HSCs) serve as the functional units of bone marrow transplantation procedures. Riddell et al. find that transplantable induced HSCs can be derived via reprogramming diverse committed blood cell types with a defined set of transcription factors. These findings demonstrate that these factors are sufficient to activate the gene networks governing HSC functional identity in committed blood cells, opening the possibility of reprogramming blood cells to derive HSCs for clinical application.

Transcriptional Network Nets Glioma Stem Cells

PAGE 580

In glioblastoma, stem-like cells that are resistant to treatment drive tumor propagation. Suvà et al. employ a multifaceted approach, combining epigenetic profiling and cellular reprogramming with functional assays in vivo, to identify a minimal set of four transcription factors that is sufficient to generate stem-like glioma cells from differentiated glioma cells. The corresponding regulatory network identifies factors required in the tumor-propagating cells, pointing to alternative therapeutic targets for eradicating this recalcitrant brain tumor.

PTEN's Passive-Aggressive Personality

PAGE 595

The PTEN tumor suppressor is frequently lost or mutated in human cancers. Papa et al. find that PTEN functions as a homodimer and that cancer-associated PTEN mutants act in a dominant-negative manner by heterodimerizing with and inhibiting the wild-type protein. The resulting reduction in PTEN function increases activation of the PI3K/Akt pathway and augments tumorigenesis.

Balancing the Budget of Protein Synthesis

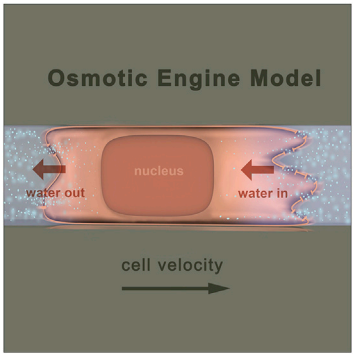
PAGE 624

Protein synthesis is energy consuming yet vital for cells. Using ribosome profiling to measure the absolute rate of protein synthesis, Li et al. now reveal how cells allocate their resources to maximize the functional output and fine-tune their biosynthetic capacity by balancing demand and supply cost. This approach provides a powerful tool for quantitative understandings of cell biology.

tRNA Biogenesis at the Heart of Neurological Disorders

PAGE 636 and PAGE 651

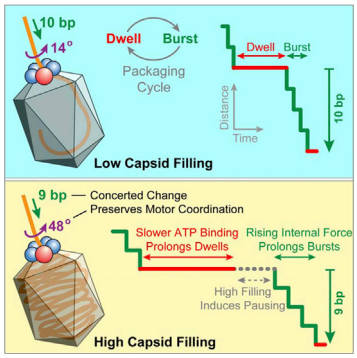
CLP1 is a multifunctional kinase implicated in tRNA, mRNA, and siRNA maturation. Karaca et al. and Schaffer et al. now identify mutations in human CLP1 in multiple families and describe the underlying complex neurological phenotypes in humans. Genetic, biochemical, and animal model approaches reveal that perturbed tRNA biogenesis associated with defective CLP1 kinase activity increases neural precursor cell susceptibility to apoptosis, implicating tRNA biogenesis in central and peripheral neurodegeneration.



Hydrodynamic Propulsion for Cells

PAGE 611

Actin and myosin-mediated contractility is considered fundamental to cell migration, yet their inhibition does not always prevent migration. Stroka et al. reveal an alternative mechanism, in which a spatial gradient of ion channels and pumps in the plasma membrane is established, creating a net inflow of water and ions at the leading edge and a net outflow at the trailing edge and thus propelling the cell forward.



Rhythm of the Ring

PAGE 702

Multimeric, ring-shaped molecular motors reply on the coordination between their subunits to perform. A viral packaging motor that rotates, translocates, and packages DNA into the capsid faces increasing internal pressure as the capsid fills. Liu et al. show that the rotation increases with filling, and this increase accompanies a reduction in the motor's step size. These concerted changes explain how this motor adjusts its operation in response to changing conditions.

Merkel Feels the Touch

PAGE 664

Ikeda et al. find that mammalian Merkel cells, previously thought to play a supportive role for the sensory nerve endings, are the primary sites of tactile transduction. The mechanosensitive ion channel Piezo2 transduces tactile stimuli into Ca^{2+}-action potentials in Merkel cells, which then drive impulses in the nerve endings to produce tactile behavioral responses. These findings show that Merkel cells are a class of specialized transducer cells encoding light touch that enable sensory tasks including tactile discrimination.

Nose Thyself

PAGE 676

Animals utilize sensory information to instruct social behavior. Kaur et al. report that a family of mouse pheromone proteins that indicate "self" versus "nonself" are processed based on their combinatory input and relative concentration ratios. This information is further integrated with additional environmental cues and past experience to influence behavioral outputs such as aggression or territorial marking.

Clock Watcher

PAGE 689

Although much is known about the cellular and molecular components of the circadian clock, the output pathways that couple clock cells to overt behaviors have remained unknown. Cavanaugh et al. identify cells of the *Drosophila* pars intercerebralis, a functional homologue of the mammalian hypothalamus, that are anatomically connected to clock cells and control circadian patterns of rest and activity through release of the corticotropin releasing factor homologue, DH44.

Wanderlust for Single-Cell Data

PAGE 714

While acquisition of single-cell data has exploded, analyzing them in a population context without losing unique information from each cell has been challenging. Bendall et al. develop Wanderlust, an algorithm that leverages single-cell data from a population and orders them along their developmental trajectory. By obtaining single-cell mass cytometry data from human bone marrow and applying Wanderlust, the authors determine the developmental progression of HSCs to naïve B cells and identify previously unknown cell states and regulatory coordination points.

Repressors, Repressors, Everywhere

PAGE 740

Kemmeren et al. present a comprehensive mRNA expression profiling study reporting the effects of over 1,400 individual gene deletions in yeast, focusing on nonessential regulators of gene expression. Their analysis indicates a surprisingly high abundance of repressors, suggesting that chromatin itself may not be as generally restrictive to transcription as previously thought. The data set also informs the architecture of protein complexes and pathways, connectivity patterns, and network circuits.

Clearing Your Head

PAGE 726

Imaging with single-cell resolution is crucial for the identification and analysis of cellular circuits in the brain. Susaki et al. report a simple method involving the immersion of samples in a chemical mixture, enabling rapid whole-brain imaging with single-photon excitation microscopy and scaling from subcellular structures to a primate brain. Using fluorescent proteins, this facilitates the visualization and quantification of neural activities induced by environmental stimulation.